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EXAMINER	
QUAN, ELIZABETH S	

ART UNIT	PAPER NUMBER
1743	

DATE MAILED: 01/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 10/03)

AS

Office Action Summary	Application No.	Applicant(s)	
	09/811,999	SHA ET AL.	
	Examiner	**Art Unit**	
	Elizabeth Quan	1743	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 14 November 2003.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-9,37,41 and 42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-9,37,41 and 42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1, 5, 6, 9 are rejected under 35 U.S.C. 102(b) as being anticipated by EP 0408280 to Norton.

Norton discloses a microplate (10) comprising a frame having a plurality of wells formed therein with each well including a plurality of first wells (15) having a relatively small reservoir with a substantially concaved bottom and second well (14) having a relatively large reservoir (figs. 2a and 2b). The first wells are not entirely located within the second well nor are the first wells entirely located outside of the second well but instead the first wells have a portion of which that overlaps the second well (figs. 2a and 2b).

The frame has a footprint sized to be handled by a robotic handling system (abstract; col. 1, lines 7-35; col. 2, lines 31-37; col. 4, lines 2-5 and 35-56). It is noted that the frame of the microplate with a footprint **sized to be handled by a robotic handling system** has not been positively recited. Therefore, the sizing of footprint of the frame to be handled by a robotic handling system is not accorded patentable weight in the claim. The prior art does not have to teach or fairly suggest the frame actually being handled by the robotic handling system since the

prior art teaches the frame with a footprint sized such that it is capable of being handled by a robotic handling system.

Each well is positioned on the frame such that a liquid handling system can automatically deposit a sample solution into the first well and reagent solution into the second well (abstract; col. 1, lines 7-35; col. 2, lines 31-37; col. 4, lines 2-5 and 35-56). It is noted that each well **positioned on the frame such that a liquid handling system can automatically deposit a sample solution into the first well and reagent solution into the second well** has not been positively recited. Therefore, the positioning of each well on the frame such that a liquid handling system can automatically deposit a sample solution into the first well and reagent solution into the second well is not accorded patentable weight in the claim. The prior art does not have to teach or fairly suggest a liquid handling system actually depositing a sample solution into the first well and reagent solution into the second well since the prior art teaches each well is positioned such that it is capable of being accessed by a liquid handling system for depositing solutions.

The frame and plurality of wells form a multi-well high-throughput plate. The recitation of a protein crystallography plate is construed as intended use (see MPEP 2111.02). A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPQ 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963).

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. Claims 5, 6, 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0408280 to Norton in view of U.S. Patent No. 5,910,287 to Cassin et al. and/or U.S. Patent No. 6,503,456 to Knebel and/or U.S. Patent No. 6,340,589 to Turner et al. and/or U.S. Patent No. 6,296,673 to Santarsiero et al.

Norton fails to disclose a Society of Biomolecular Screening compatible robotic handling system handling a frame. However, Cassin et al. disclose that the footprint of a standard 96-well microtiter plate is 12.7 in length and 8.5 cm in width (see COL. 8, lines 55-57). The generally accepted standard footprint for a standard 96-well microtiter plate for robotics application has a length of 12.77 +/- 0.25 cm and width of 8.55 +/- 0.25 cm (see COL. 8, lines 55-63). These standards are within the ranges of the Society of Biomolecular Screening standards, as stipulated in the immediate application. Knebel also discloses a microplate (1) with a frame (2) that

complies with the Society of Biomolecular Screening standards (see COL. 5, lines 22-27). Turner et al. also disclose that standardizing the features of the microplate according to Society of Biomolecular Screening standards are recommended in the successful deployment of microplates in robotic handling and liquid handling instruments (see COL. 2, lines 8-18). Santarsiero et al. disclose a robotic handling system, including transportation of the microplates and liquid distribution of solutions into the wells of the microplates (see FIGS. 1, 4D, 4E, 4F, 4H, 5A, 5B, 5C, 6; COL. 8, line 67; COLS. 9 and 10). Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the microplate of Norton to make the frame with a certain footprint and well positioning that is handled by a Society of Biomolecular Screening compatible robotic handling system as in Cassin et al. and/or Knebel and/or Turner et al. and/or Santarsiero et al. to conform with very well known and accepted standards to ensure the availability of robots that can work with the microplate.

Norton fails to disclose that the frame along with the plurality of wells is made from cyclo-olefin. However, Cassin et al. disclose that at least a portion of a bottom surface of a well of the plate is made from cyclo-olefin or substantially the entire bottom to facilitate ease of manufacture (see COL. 6, lines 35-39). Cyclo-olefin can also be used to form the walls of the plate, which is another way of reducing the inherent fluorescence of the plate (see COL. 6, lines 39-41). Cyclo-olefin may optionally comprise any portion of a plate, including the plate bottom, well walls, inter-well structural members that interconnect the wells, plate sides, plate upper or lower surfaces, as well as plate lids (see COL. 6, lines 42-46). Therefore, it would have been obvious to modify the microplate of Norton to make the frame from cyclo-olefin as in Cassin et al. to reduce the inherent fluorescence of the plate and facilitate ease of manufacture to make the

entire microplate assembly from cyclo-olefin since the bottom and walls of the plate are made from cyclo-olefin.

4. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0408280 to Norton in view of U.S. Patent No. 5,096,676 to McPherson et al. or U.S. Patent No. 5,604,130 to Warner et al.

Norton fails to disclose a seal is positioned over the plurality of wells. However, McPherson et al. a seal (34) to seal the wells from the atmosphere making it conducive to the vapor diffusion process for generating crystals (see COL. 4, lines 3-16; COL. 5, lines 5-25). Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the microplate of the Norton to include a seal positioned over the plurality of wells to seal the wells from the atmosphere to induce vapor diffusion for generating crystals as taught by McPherson et al. or prevent loss of well contents during heating or agitation as taught by Warner et al. (cols. 1 and 2).

5. Claims 1, 5-7, 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Applicant's Admitted Prior Art (FIGS. 2a-c) in view of U.S. Patent No. 5,096,676 to McPherson et al. or U.S. Patent No. 6,063,282 to Moulton.

The Admitted Prior Art (figs. 2a-c) discloses a 96-well high-throughput protein crystallization microplate (200) comprising a frame (204) having a plurality of wells formed therein with each well including a plurality of first wells (216), each of which has a relatively small reservoir for receiving a protein and reagent solution, and second well (214), which has a relatively large reservoir for receiving a reagent solution of higher concentration than the reagent solutions within the small reservoirs (figs. 2a-c). The first wells are not entirely located within

the second well nor are the first wells entirely located outside the second well but instead the first wells have a portion of which that overlaps the second well (figs. 2a-c; sections [0008] and [0009]). The first and second wells share a wall of lesser height than the other walls of the second well, such that the space formed by the shortened wall is the region in which the first and second wells overlap. The configuration of the plate enables the protein and reagent solution within each of the small reservoirs to interact within the reagent solution within the large reservoir via a vapor diffusion process for the formation of protein crystals within each of the small reservoirs (sections [0008] and [0009]).

The frame has a footprint sized to be handled by a robotic handling system (figs. 2a-c). It is noted that the frame of the microplate with a footprint **sized to be handled by a robotic handling system** has not been positively recited. Therefore, the sizing of footprint of the frame to be handled by a robotic handling system is not accorded patentable weight in the claim. The prior art does not have to teach or fairly suggest the frame actually being handled by the robotic handling system since the prior art teaches the frame with a footprint sized such that it is capable of being handled by a robotic handling system.

Each well is positioned on the frame such that a liquid handling system can automatically deposit a sample into the first well and reagent solution into the second well. It is noted that each well **positioned on the frame such that a liquid handling system can automatically deposit a sample solution into the first well and reagent solution into the second well** has not been positively recited. Therefore, the positioning of each well on the frame such that a liquid handling system can automatically deposit a sample solution into the first well and reagent solution into the second well is not accorded patentable weight in the claim. The prior art does

not have to teach or fairly suggest a liquid handling system actually depositing a sample solution into the first well and reagent solution into the second well since the prior art teaches each well positioned such that it is capable of being accessed by a liquid handling system for depositing solutions.

The Admitted Prior Art (figs. 2a-c) fails to disclose that the first wells have a relatively small reservoir with a substantially concaved bottom. However, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the plate of the Admitted Prior Art (figs. 2a-c) to include first wells having a relatively small reservoir with a substantially concaved bottom to accommodate the particular protein drop being crystallized when using lower surface tension solutions as taught by McPherson et al. (col. 4, lines 52-58) and so that material will tend to collect in the center of the bottom of the reservoir or well as taught by Moulton (see col. 2, lines 53-55). Furthermore, it has been held that change in form or shape is an obvious engineering design (*In re Dailey*, 149 USPQ 47 (CCPA 1976)).

Applicant's admitted prior art does not address whether a seal is positioned over the plurality of wells. However, McPherson et al. a seal (34) to seal the wells from the atmosphere making it conducive to the vapor diffusion process for generating crystals (see COL. 4, lines 3-16; COL. 5, lines 5-25). Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the microplate of the Applicant's admitted prior art to include a seal positioned over the plurality of wells as in McPherson et al. to seal the wells from the atmosphere to induce vapor diffusion for generating crystals.

6. Claims 37, 41, 42 rejected under 35 U.S.C. 103(a) as being unpatentable over Applicant's Admitted Prior Art (FIGS. 2a-c) in view of U.S. Patent No. 5,096,676 to McPherson et al. or

U.S. Patent No. 6,063,282 to Moulton., and further in view of U.S. Patent No. 5,910,287 to Cassin et al. and/or U.S. Patent No. 6,503,456 to Knebel and/or U.S. Patent No. 6,340,589 to Turner et al. and/or U.S. Patent No. 6,296,673 to Santarsiero et al.

The Admitted Prior Art (figs. 2a-c) discloses a microplate (200) comprising a frame (204) having a plurality of wells formed therein with each well including a plurality of first wells (216), each of which has a relatively small reservoir for receiving a protein and reagent solution, and second well (214), which has a relatively large reservoir for receiving a reagent solution of higher concentration than the reagent solutions within the small reservoirs (figs. 2a-c). The first wells are not entirely located within the second well nor are the first wells entirely located outside the second well but instead the first wells have a portion of which that overlaps the second well (figs. 2a-c; sections [0008] and [0009]). The first and second wells share a wall of lesser height than the other walls of the second well, such that the space formed by the shortened wall is the region in which the first and second wells overlap. The configuration of the plate enables the protein and reagent solution within each of the small reservoirs to interact within the reagent solution within the large reservoir via a vapor diffusion process for the formation of protein crystals within each of the small reservoirs (sections [0008] and [0009]).

The frame has a footprint sized to be handled by a robotic handling system (figs. 2a-c). It is noted that the frame of the microplate with a footprint **sized to be handled by a robotic handling system** has not been positively recited. Therefore, the sizing of footprint of the frame to be handled by a robotic handling system is not accorded patentable weight in the claim. The prior art does not have to teach or fairly suggest the frame actually being handled by the robotic

handling system since the prior art teaches the frame with a footprint sized such that it is capable of being handled by a robotic handling system.

Each well is positioned on the frame such that a liquid handling system can automatically deposit a sample into the first well and reagent solution into the second well. It is noted that each well **positioned on the frame such that a liquid handling system can automatically deposit a sample solution into the first well and reagent solution into the second well** has not been positively recited. Therefore, the positioning of each well on the frame such that a liquid handling system can automatically deposit a sample solution into the first well and reagent solution into the second well is not accorded patentable weight in the claim. The prior art does not have to teach or fairly suggest a liquid handling system actually depositing a sample solution into the first well and reagent solution into the second well since the prior art teaches each well positioned such that it is capable of being accessed by a liquid handling system for depositing solutions.

The Admitted Prior Art (figs. 2a-c) fails to disclose that the first wells have a relatively small reservoir with a substantially concaved bottom. However, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the plate of the Admitted Prior Art (figs. 2a-c) to include first wells having a relatively small reservoir with a substantially concaved bottom to accommodate the particular protein drop being crystallized when using lower surface tension solutions as taught by McPherson et al. (col. 4, lines 52-58) and so that material will tend to collect in the center of the bottom of the reservoir or well as taught by Moulton (see col. 2, lines 53-55). Furthermore, it has been held that change in form or shape is an obvious engineering design (*In re Dailey*, 149 USPQ 47 (CCPA 1976)).

Norton fails to disclose a Society of Biomolecular Screening compatible robotic handling system handling a frame. However, Cassin et al. disclose that the footprint of a standard 96-well microtiter plate is 12.7 in length and 8.5 cm in width (see COL. 8, lines 55-57). The generally accepted standard footprint for a standard 96-well microtiter plate for robotics application has a length of 12.77 +/- 0.25 cm and width of 8.55 +/- 0.25 cm (see COL. 8, lines 55-63). These standards are within the ranges of the Society of Biomolecular Screening standards, as stipulated in the immediate application. Knebel also discloses a microplate (1) with a frame (2) that complies with the Society of Biomolecular Screening standards (see COL. 5, lines 22-27). Turner et al. also disclose that standardizing the features of the microplate according to Society of Biomolecular Screening standards are recommended in the successful deployment of microplates in robotic handling and liquid handling instruments (see COL. 2, lines 8-18). Santarsiero et al. disclose a robotic handling system, including transportation of the microplates and liquid distribution of solutions into the wells of the microplates (see FIGS. 1, 4D, 4E, 4F, 4H, 5A, 5B, 5C, 6; COL. 8, line 67; COLS. 9 and 10). Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the microplate of Norton to make the frame with a certain footprint and well positioning that is handled by a Society of Biomolecular Screening compatible robotic handling system as in Cassin et al. and/or Knebel and/or Turner et al. and/or Santarsiero et al. to conform with very well known and accepted standards to ensure the availability of robots that can work with the microplate.

Norton fails to disclose that the frame along with the plurality of wells is made from cyclo-olefin. However, Cassin et al. disclose that at least a portion of a bottom surface of a well of the plate is made from cyclo-olefin or substantially the entire bottom to facilitate ease of

manufacture (see COL. 6, lines 35-39). Cyclo-olefin can also be used to form the walls of the plate, which is another way of reducing the inherent fluorescence of the plate (see COL. 6, lines 39-41). Cyclo-olefin may optionally comprise any portion of a plate, including the plate bottom, well walls, inter-well structural members that interconnect the wells; plate sides, plate upper or lower surfaces, as well as plate lids (see COL. 6, lines 42-46). Therefore, it would have been obvious to modify the microplate of Norton to make the frame from cyclo-olefin as in Cassin et al. to reduce the inherent fluorescence of the plate and facilitate ease of manufacture to make the entire microplate assembly from cyclo-olefin since the bottom and walls of the plate are made from cyclo-olefin.

7. Claims 37, 41, 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0408280 to Norton in view of U.S. Patent No. 5,910,287 to Cassin et al. and/or U.S. Patent No. 6,503,456 to Knebel and/or U.S. Patent No. 6,340,589 to Turner et al. and/or U.S. Patent No. 6,296,673 to Santarsiero et al.

Norton discloses a microplate (10) comprising a frame having a plurality of wells formed therein with each well including a plurality of first wells (15) having a relatively small reservoir with a substantially concaved bottom and second well (14) having a relatively large reservoir (figs. 2a and 2b). The first wells are not entirely located within the second well nor are the first wells entirely located outside of the second well but instead the first wells have a portion of which that overlaps the second well (figs. 2a and 2b).

The frame has a footprint sized to be handled by a robotic handling system (abstract; col. 1, lines 7-35; col. 2, lines 31-37; col. 4, lines 2-5 and 35-56). It is noted that the frame of the microplate with a footprint **sized to be handled by a robotic handling system** has not been

positively recited. Therefore, the sizing of footprint of the frame to be handled by a robotic handling system is not accorded patentable weight in the claim. The prior art does not have to teach or fairly suggest the frame actually being handled by the robotic handling system since the prior art teaches the frame with a footprint sized such that it is capable of being handled by a robotic handling system.

Each well is positioned on the frame such that a liquid handling system can automatically deposit a sample solution into the first well and reagent solution into the second well (abstract; col. 1, lines 7-35; col. 2, lines 31-37; col. 4, lines 2-5 and 35-56). It is noted that each well **positioned on the frame such that a liquid handling system can automatically deposit a sample solution into the first well and reagent solution into the second well** has not been positively recited. Therefore, the positioning of each well on the frame such that a liquid handling system can automatically deposit a sample solution into the first well and reagent solution into the second well is not accorded patentable weight in the claim. The prior art does not have to teach or fairly suggest a liquid handling system actually depositing a sample solution into the first well and reagent solution into the second well since the prior art teaches each well is positioned such that it is capable of being accessed by a liquid handling system for depositing solutions.

The first wells each with a relatively small reservoir is capable of receiving a protein and reagent solution, and the second well with a relatively large reservoir is capable of receiving a reagent solution of higher concentration than that of the reagent solution in the first wells. It is noted that a first well including a relatively small reservoir having a substantially concaved bottom **for receiving a protein solution and a reagent solution**; and a second well including a

relatively large reservoir **for receiving a reagent solution that has a higher concentration that the reagent solution within the first well** has not been positively recited. Therefore, the limitations are not accorded patentable weight in the claim. The prior art does not have to teach or fairly suggest the first wells actually containing a protein solution and reagent solution and the second well actually containing a reagent solution higher in concentration than that of the reagent solution in the first well since the prior art teaches first and second wells capable of receiving these specific solutions.

The frame and plurality of wells form a multi-well high-throughput plate. The recitation of a protein crystallography plate is construed as intended use (see MPEP 2111.02). A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPQ 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963).

Norton fails to disclose a Society of Biomolecular Screening compatible robotic handling system handling a frame. However, Cassin et al. disclose that the footprint of a standard 96-well microtiter plate is 12.7 in length and 8.5 cm in width (see COL. 8, lines 55-57). The generally accepted standard footprint for a standard 96-well microtiter plate for robotics application has a length of 12.77 +/- 0.25 cm and width of 8.55 +/- 0.25 cm (see COL. 8, lines 55-63). These standards are within the ranges of the Society of Biomolecular Screening standards, as stipulated in the immediate application. Knebel also discloses a microplate (1) with a frame (2) that

complies with the Society of Biomolecular Screening standards (see COL. 5, lines 22-27). Turner et al. also disclose that standardizing the features of the microplate according to Society of Biomolecular Screening standards are recommended in the successful deployment of microplates in robotic handling and liquid handling instruments (see COL. 2, lines 8-18). Santarsiero et al. disclose a robotic handling system, including transportation of the microplates and liquid distribution of solutions into the wells of the microplates (see FIGS. 1, 4D, 4E, 4F, 4H, 5A, 5B, 5C, 6; COL. 8, line 67; COLS. 9 and 10). Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the microplate of Norton to make the frame with a certain footprint and well positioning that is handled by a Society of Biomolecular Screening compatible robotic handling system as in Cassin et al. and/or Knebel and/or Turner et al. and/or Santarsiero et al. to conform with very well known and accepted standards to ensure the availability of robots that can work with the microplate.

Norton fails to disclose that the frame along with the plurality of wells is made from cyclo-olefin. However, Cassin et al. disclose that at least a portion of a bottom surface of a well of the plate is made from cyclo-olefin or substantially the entire bottom to facilitate ease of manufacture (see COL. 6, lines 35-39). Cyclo-olefin can also be used to form the walls of the plate, which is another way of reducing the inherent fluorescence of the plate (see COL. 6, lines 39-41). Cyclo-olefin may optionally comprise any portion of a plate, including the plate bottom, well walls, inter-well structural members that interconnect the wells, plate sides, plate upper or lower surfaces, as well as plate lids (see COL. 6, lines 42-46). Therefore, it would have been obvious to modify the microplate of Norton to make the frame from cyclo-olefin as in Cassin et al. to reduce the inherent fluorescence of the plate and facilitate ease of manufacture to make the

entire microplate assembly from cyclo-olefin since the bottom and walls of the plate are made from cyclo-olefin.

8. Alternatively, Claims 37, 41, 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0408280 to Norton in view of U.S. Patent No. 5,910,287 to Cassin et al. and/or U.S. Patent No. 6,503,456 to Knebel and/or U.S. Patent No. 6,340,589 to Turner et al. and/or U.S. Patent No. 6,296,673 to Santarsiero et al., and further in view of WO 00/00678 to Hol et al.

Norton discloses that the microplate can be used for different assays. Norton in view of Cassin et al. and/or Knebel and/or Turner et al. and/or Santarsiero et al. fail to disclose the plate is used for forming protein crystals. However, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the microplate of Norton in view of Cassin et al. and/or Knebel and/or Turner et al. and/or Santarsiero et al. to use the plate in a particular assay, such as protein crystallization wherein the first wells each with a relatively small reservoir receives a protein and reagent solution, the second well with a relatively large reservoir receives a reagent solution of higher concentration than that of the reagent solution in the first wells, and the contents of the wells interact by a vapor diffusion process as desired or necessary in crystallization experimentations toward the advancement of drugs and molecular biology.

9. Claims 1, 5-7, 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/00678 to Hol et al. in view of U.S. Patent No. 5,096,676 to McPherson et al.

Hol et al. disclose a 96-well high-throughput protein crystallization plate (10) comprising a frame (12) with a plurality of wells (26) formed therein (see ABSTRACT; FIGS. 1 and 2;

PAGE 19, lines 1-8). Each well (26) includes a first well (32) with a relatively small reservoir and second well (28) with a relatively large reservoir positioned near the relatively small reservoir of the first well (32) (see FIGS. 1 and 2; PAGE 19, lines 1-8). The first and second wells share a wall of lesser height than the other walls of the second well, such that the space formed by the shortened wall, which is labeled as the diffusion channel, is the region in which the first and second wells overlap. The configuration of the plate enables the protein and reagent solution within each of the small reservoirs to interact within the reagent solution within the large reservoir via a vapor diffusion process for the formation of protein crystals within each of the small reservoirs (sections [0008] and [0009]). The frame and plurality of wells is a 96 well high-throughput protein crystallography plate (see FIGS. 1 and 2).

The frame of the microplate has a footprint that is capable of being handled by a robotic handling system (figs. 1 and 2). It is noted that the frame of the microplate with a footprint **sized to be handled by a robotic handling system** has not been positively recited. Therefore, the sizing of footprint of the frame to be handled by a robotic handling system is not accorded patentable weight in the claim. The prior art does not have to teach or fairly suggest the frame actually being handled by the robotic handling system since the prior art teaches the frame with a footprint sized such that it is capable of being handled by a robotic handling system.

Each well is positioned on the frame, such that a liquid handling system can automatically deposit a sample solution into the first well and reagent solution into the second well (figs. 1 and 2). It is noted that each well **positioned on the frame such that a liquid handling system can automatically deposit a sample solution into the first well and reagent solution into the second well** has not been positively recited. Therefore, the positioning of each

well on the frame such that a liquid handling system can automatically deposit a sample solution into the first well and reagent solution into the second well is not accorded patentable weight in the claim. The prior art does not have to teach or fairly suggest a liquid handling system actually depositing a sample solution into the first well and reagent solution into the second well since the prior art teaches each well positioned such that it is capable of being accessed by a liquid handling system for depositing solutions.

Hol et al. disclose in EXAMPLE 1 that the first well or drop chamber (32) receives two microliters of the crystallization from the second well or central chamber/reservoir (28) (see PAGE 20, lines 8-10). Two microliters of dissolved protein is mixed with the two microliters of crystallization solution in the first well or drop chamber (32), and the crystallization chambers were sealed with Crystal Clear tap (see PAGE 20, lines 10-12). The dissolved protein was made by: 1) adding 1M ammonium hydroxide to a protein slurry until the solution becomes transparent, 2) adjusting the solution to 200 mM sodium chloride by the addition of 5 M sodium chloride stock solution, and 3) adjusting the solution to pH 7.0 by addition of 0.1 M hydrochloric acid (see PAGE 19, lines 29-35; PAGE 20, lines 1-5). The final concentration of protein was determined to be 30 milligrams per millimeter, which is equivalent to 0.03 gram per milliliter or 3 grams per 100 milliliters or 3% (w/v) protein solution (see PAGE 20, lines 1 and 2). The protein crystallized in solution number 8 of Solution Set III or Table III (see PAGE 9). Solution number 8 is made of 2.0 M $(NH_4)_2SO_4$ or 26.4% (w/v) $(NH_4)_2SO_4$ using the molecular weight 132.1342 grams per mole of $(NH_4)_2SO_4$ (see PAGE 9). Solution number 8 may optionally contain 0.1 M buffer (see PAGE 9; PAGE 14, lines 10-13). In EXAMPLE 2 a protein solution has a concentration of 2% (see PAGE 20, lines 21 and 22). The protein crystallized in solution

number 28 of Solution Set III or Table III (see PAGE 10). Solution number 28 is made of 20% (w/v) PEG-8000 (see PAGE 10). Solution number 28 may optionally contain 0.1 M HEPES pH 7.5 (see PAGE 10; PAGE 14, lines 13-15). It is noted that when two microliters of the protein solution is mixed with the two microliters of crystallization solution, the overall solution containing the protein solution and crystallization solution, as well as the protein, the reagents used to create the protein solution, and the added reagent or crystallization solution, would be diluted or have a lesser concentration such that the reagent or crystallization solution added to the protein would have a lower concentration than the original reagent or crystallization solution. Additionally, the specification on page 23, lines 1-5 states that the uneven concentration between the reagent solution in the first well and the reagent solution in the second well drives a natural vapor diffusion process towards equilibrium. Since vapor diffusion process occurs and reaches equilibrium by forming protein crystals in the first well or drop chamber in Hol et al., it would appear the reagents used in Hol et al. have an uneven concentration, where the reagents in second well has a higher concentration than the reagents in the first well (see PAGE 1, lines 23 and 24; PAGE 2, lines 1 and 2; PAGE 15, lines 5-35; PAGE 16, lines 1-35; PAGE 17, lines 1-35; PAGE 18, lines 1-35).

In Hol et al. it is unclear whether the bottoms of each of the relatively small reservoirs of the first wells are concaved. However, McPherson et al. disclose the relatively small reservoir of the first well (30) with a substantially concaved bottom (see 53-58). The first well (30) can be formed of an optimum size and shape to accommodate the particular protein drop being crystallized (see COL. 4, lines 52-55). When lower surface tension solutions, including protein solutions containing detergents are used, a cup-shaped receptacle or a receptacle with a

substantially concaved bottom has proven satisfactory (see COL. 4, lines 55-58). Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the microplate of Hol et al. to make the relatively small reservoir of the first well with a substantially concaved bottom as in McPherson et al. to accommodate the particular protein drop being crystallized when using lower surface tension solutions.

Hol et al. fail to disclose a seal positioned over the plurality of wells. However, McPherson et al. a seal (34) to seal the wells from the atmosphere making it conducive to the vapor diffusion process for generating crystals (see COL. 4, lines 3-16; COL. 5, lines 5-25). Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the microplate of Hol et al. to include a seal positioned over the plurality of wells as in McPherson et al. to seal the wells from the atmosphere to induce vapor diffusion for generating crystals.

10. Claims 5, 6, 8, 37, 41, 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/00678 to Hol et al. in view of U.S. Patent No. 5,096,676 to McPherson et al. in view of U.S. Patent No. 5,910,287 to Cassin et al. and/or U.S. Patent No. 6,503,456 to Knebel and/or U.S. Patent No. 6,340,589 to Turner et al. and/or U.S. Patent No. 6,296,673 to Santarsiero et al.

Hol et al. in view of McPherson et al. do not explicitly disclose a Society of Biomolecular Screening compatible robotic handling system handling a frame. However, Cassin et al. disclose that the footprint of a standard 96-well microtiter plate is 12.7 in length and 8.5 cm in width (see COL. 8, lines 55-57). The generally accepted standard footprint for a standard 96-well microtiter plate for robotics application has a length of 12.77 +/- 0.25 cm and width of 8.55 +/- 0.25 cm (see COL. 8, lines 55-63). These standards are within the ranges of the Society of Biomolecular

Screening standards, as stipulated in the immediate application. Knebel also discloses a microplate (1) with a frame (2) that complies with the Society of Biomolecular Screening standards (see COL. 5, lines 22-27). Turner et al. also disclose that standardizing the features of the microplate according to Society of Biomolecular Screening standards are recommended in the successful deployment of microplates in robotic handling and liquid handling instruments (see COL. 2, lines 8-18). Santarsiero et al. disclose a robotic handling system, including transportation of the microplates and liquid distribution of solutions into the wells of the microplates (see FIGS. 1, 4D, 4E, 4F, 4H, 5A, 5B, 5C, 6; COL. 8, line 67; COLS. 9 and 10). Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the microplate of Hol et al. in view of McPherson et al. to make the frame with a certain footprint and well positioning that is handled by a Society of Biomolecular Screening compatible robotic handling system as in Cassin et al. and/or Knebel and/or Turner et al. and/or Santarsiero et al. to conform with very well known and accepted standards to ensure the availability of robots that can work with the microplate.

Hol et al. in view of McPherson et al. do not disclose that the frame along with the plurality of wells is made from cyclo-olefin. However, Cassin et al. disclose that at least a portion of a bottom surface of a well of the plate is made from cyclo-olefin or substantially the entire bottom to facilitate ease of manufacture (see COL. 6, lines 35-39). Cyclo-olefin can also be used to form the walls of the plate, which is another way of reducing the inherent fluorescence of the plate (see COL. 6, lines 39-41). Cyclo-olefin may optionally comprise any portion of a plate, including the plate bottom, well walls, inter-well structural members that interconnect the wells, plate sides, plate upper or lower surfaces, as well as plate lids (see COL. 6, lines 42-46).

Therefore, it would have been obvious to modify the microplate of Hol et al. in view of McPherson et al. to make the frame from cyclo-olefin as in Cassin et al. to reduce the inherent fluorescence of the plate and facilitate ease of manufacture to make the entire microplate assembly from cyclo-olefin since the bottom and walls of the plate are made from cyclo-olefin.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Quan whose telephone number is (571) 272-1261. The examiner can normally be reached on M-F (8:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on (571) 272-1267. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0661.

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